

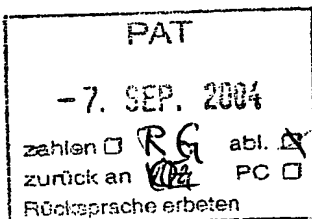
PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To:

MERCK PATENT GMBH
Frankfurter Strasse 250
D-64293 Darmstadt
ALLEMAGNE



NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing
(day/month/year)

06.09.2004

Applicant's or agent's file reference
P02/186VE/RG

IMPORTANT NOTIFICATION

International application No.
PCT/EP 03/09680

International filing date (day/month/year)
01.09.2003

Priority date (day/month/year)
07.10.2002

Applicant
MERCK PATENT GMBH

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international
preliminary examining authority:



European Patent Office
D-80298 Munich
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Authorized Officer

Brell, S

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P02/186VE/RG	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/EP 03/09680	International filing date (<i>day/month/year</i>) 01.09.2003	Priority date (<i>day/month/year</i>) 07.10.2002
International Patent Classification (IPC) or both national classification and IPC C07D313/08		
Applicant MERCK PATENT GMBH		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

I ☒ Basis of the opinion

II ☐ Priority

III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability



IV ☐ Lack of unity of invention

V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

VI ☐ Certain documents cited

VII ☐ Certain defects in the international application

VIII ☐ Certain observations on the international application

Date of submission of the demand 08.04.2004	Date of completion of this report 06.09.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Samsam Bakhtiary, M Telephone No. +49 89 2399-8556 <div style="text-align: right;">  </div>

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/09680**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*):

Description, Pages

1-14 as originally filed

Claims, Numbers

1-14 as originally filed

Drawings, Sheets

1/6-6/6 received on 21.07.2004 with letter of 15.07.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/09680**

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-14
Inventive step (IS)	Yes: Claims	
	No: Claims	1-14
Industrial applicability (IA)	Yes: Claims	1-14
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document:

D1: FR-A-2 787 789

2. **Novelty** (article 33.2 PCT)

a) concerning claims 1,3,13,14

The subject matter of claim 1 which consists in derivatives of benzoxepine cannot be considered as novel when $n=0$ or 2, and when $n=1$ the compounds containing an R being different than methoxy group.

Examples 21b,22b and 32b of document D1 anticipate the subject matter of claims 1,3,13 and 14.

The fact that the wording of the claim contains "metastable form" does not render the said compounds novel. It is necessary that metastable form of a compound distinguishes itself from the stable form by technical features (such as IR, X-ray diffraction...).

b) concerning claims 2,4-12

As far as subject matter of claim 2 is concerned, the Applicant is invited to provide IR spectra, X-ray diffraction of the stable corresponding form of the compounds of claim 2 and this in order to put forward that the stable and metastable form have distinct crystalline structures, if such evidence is not provided, then novelty issue may be reconsidered.

The Applicant with his letter of 15.07.2004, provided experimental data's which in fact were disclosed in the in the original filing (priority).

These data's concern the metastable form, in our written opinion, we drew the attention of the Applicant to the fact that the data's for the stable form was necessary in order to put forward distinctive features for recognising novelty requirements.

Therefore novelty for claims 2,4-12 cannot be recognised.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/09680

2. Inventive step (article 33.3 PCT)

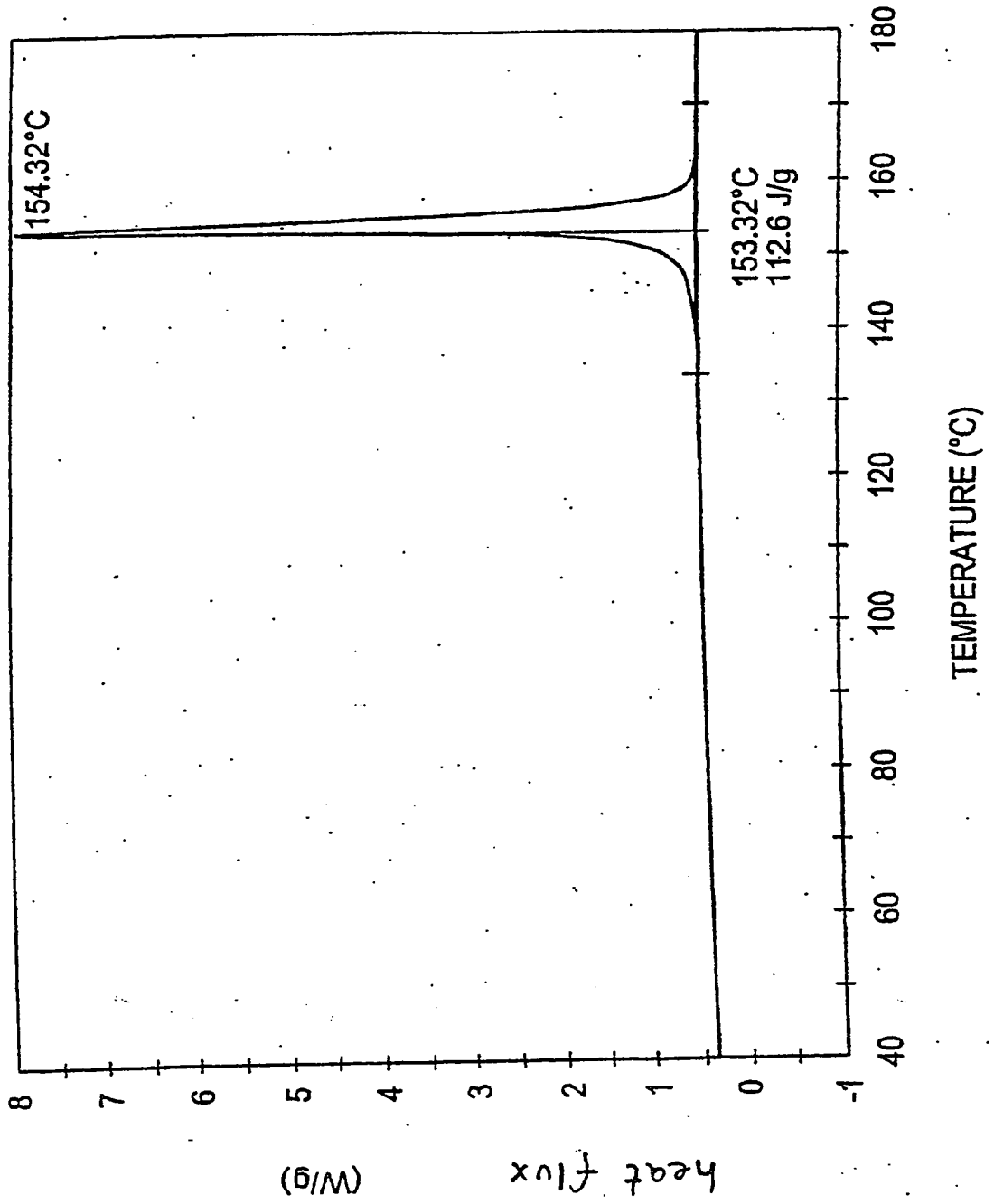
Since novelty cannot be recognised for the claimed subject matter, then this subject matter cannot be considered as inventive.

In the european phase, in case novelty can be re-established by appropriate amendments or convincing experimental data's, then inventivity could be recognised for this novel subject matter for the following reasons:

The problem to be solved by this application can be regarded as to put forward benzoxepine derivatives having improved dissolution kinetics.

The proposed solution, namely making a metastable form seems to solve the problem. The comparative tests disclosed in the description of this application indeed show that the compounds in the metastable form possess specific surfaces superior than those in stable form, such improvement was not obviously derivable from the state of the art.

FIG.1



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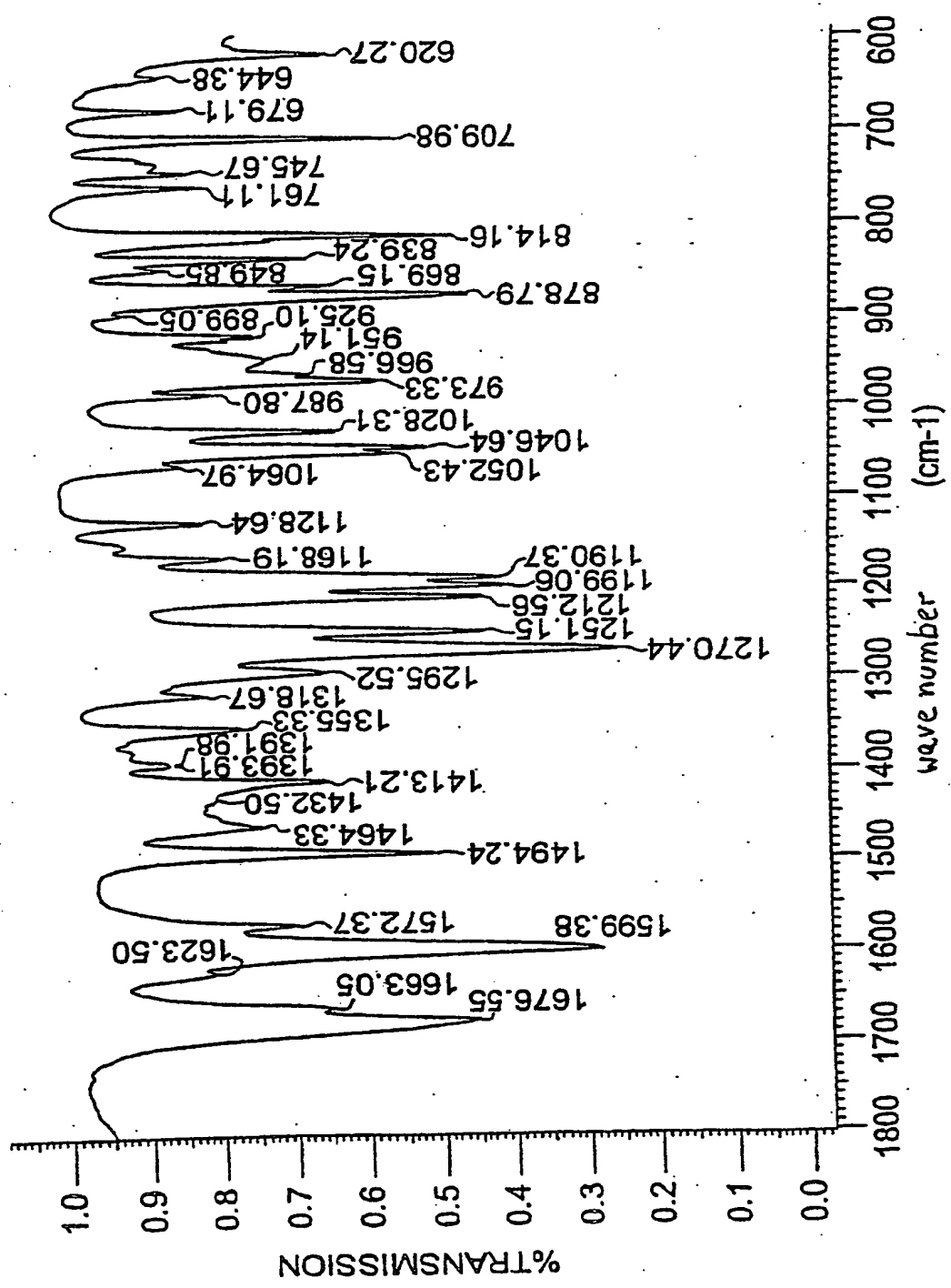
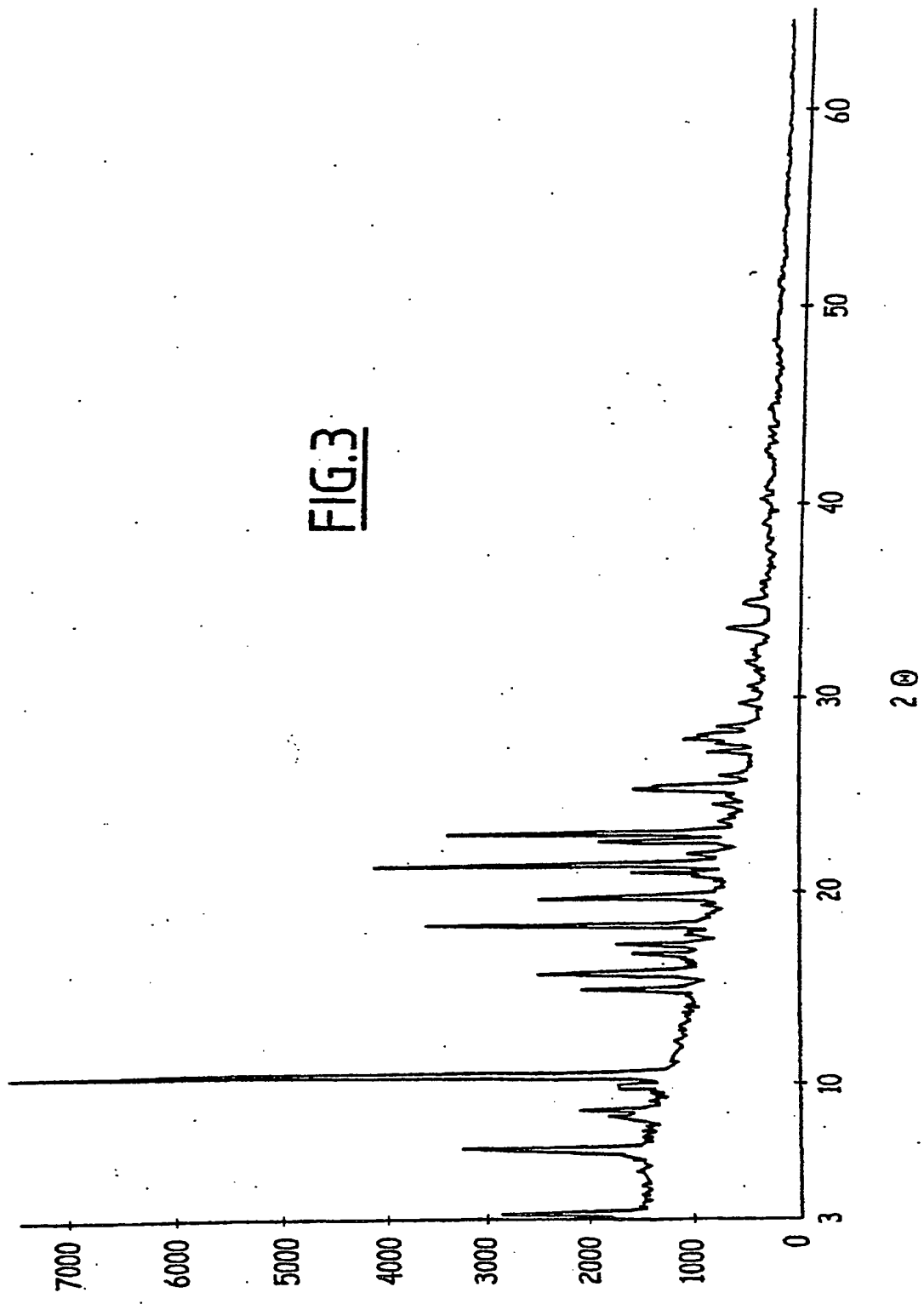


FIG.2

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FIG.3



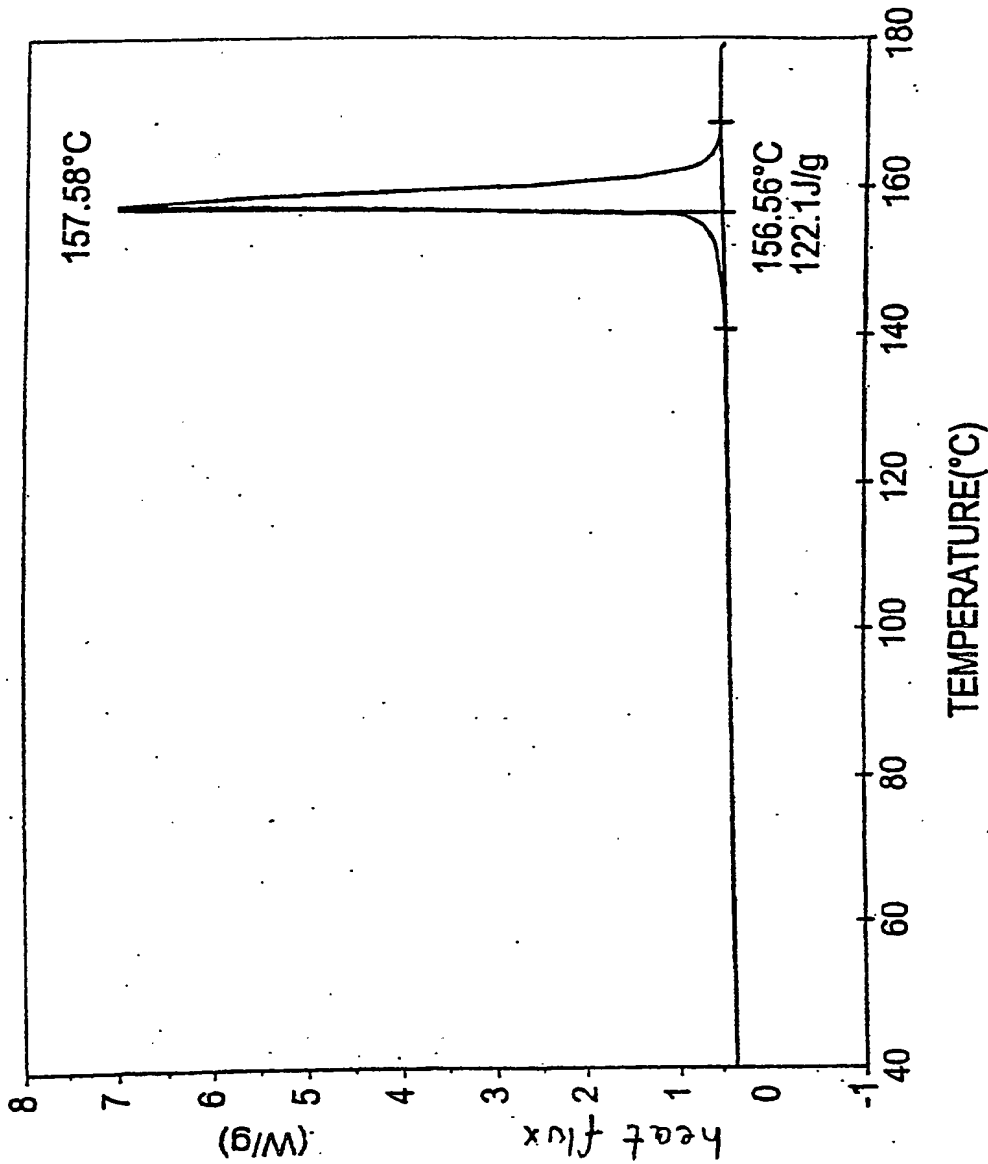


FIG.4

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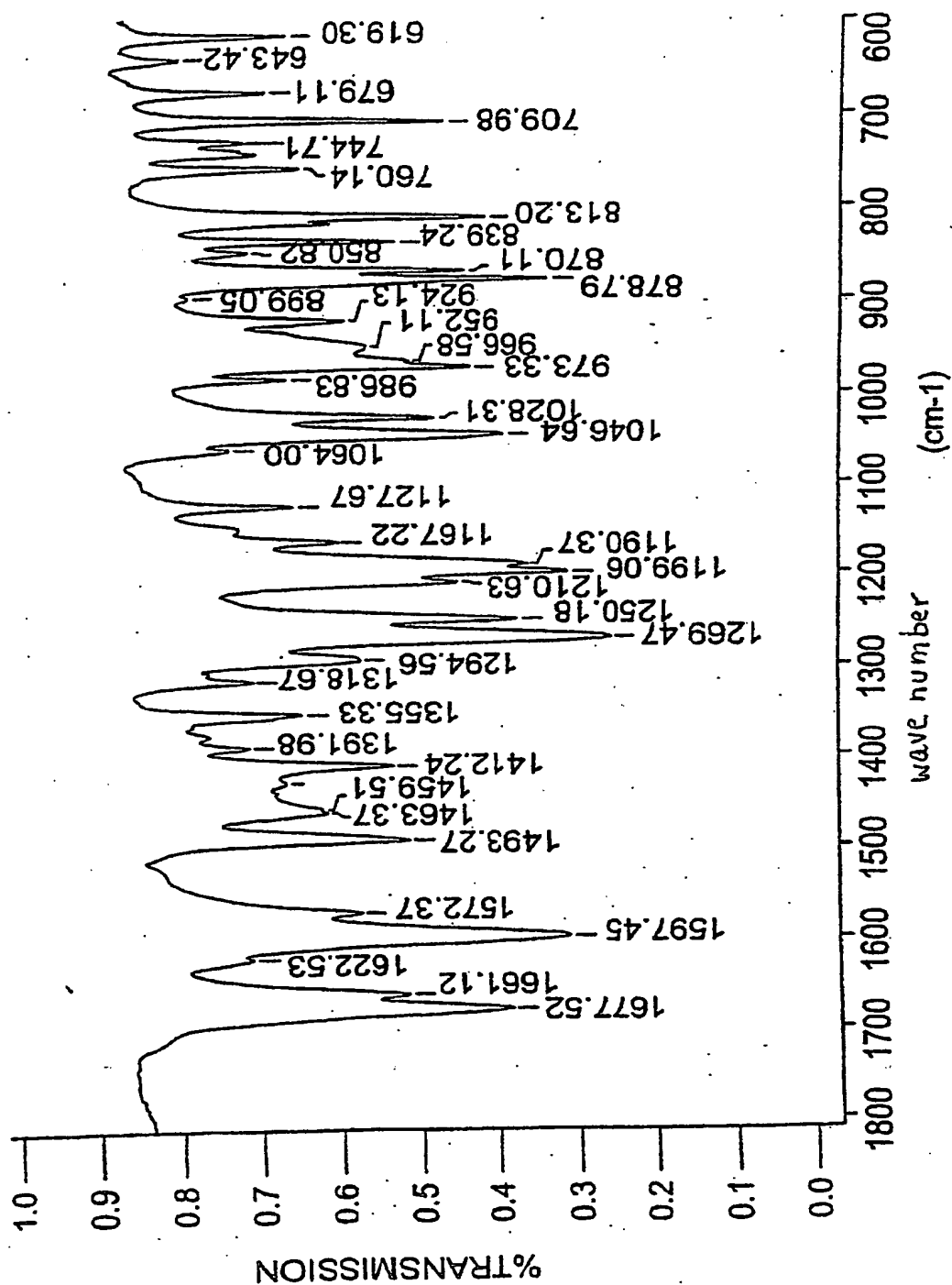


FIG.5

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